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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,592	03/11/2004	Robert A. Herrmann	00-0193US02	6360

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EXAMINER	
GHALI, ISIS A D	

ART UNIT	PAPER NUMBER
1611	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/798,592	HERRMANN ET AL.	
	Examiner	Art Unit	
	Isis A. Ghali	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *23-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22, 40-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The receipt is acknowledged of applicants' amendment filed 07/15/2009.

Claims 1- 41 are pending.

Claims 23-39 are withdrawn from further consideration as being drawn to a nonelected inventions and species. Election was made **without** traverse in the reply filed on 08/22/2007.

Claims 1-22 40 and 41 are included in the prosecution.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1-22 and 40-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,087,479 ('479) combined with the article "S-Nitrosothiols cause prolonged, nitric oxide mediated relaxation in human saphenous vein and internal mammary artery: therapeutic potential in bypass surgery" by Sogo et al.

US '479 teaches a medical device that may be made such that at least a portion of it which come in contact with blood or vascular tissue includes nitric oxide adduct (col.9, lines 48-52). The nitric oxide adduct can be incorporated into synthetic or natural matrix which is then used to coat those same contact surfaces of the device (col.9, lines 57-60). Therefore, the nitric oxide adduct can be incorporated in portion of the vascular device and also in the coating of the same device, i.e. two different matrices, which are expected to be different. The nitric oxide adducts include S-nitrosylated compounds such as nitrosylated amino acid, sydnonimines, and organic nitrate (col.5, lines 1-5, 18-22; col.10, lines 41-56). The polymeric matrix includes polylactic acid (col.3, line 65-col.4, line 15; col.9, lines 57-59; col.10, lines 1-2). The reference disclosed that the material of the medical device different from the coating matrix. The medical devices of the invention can be vascular devices, such as catheter, heart valve (col.3, lines 59-62).

Although the reference teaches many different NO adducts and teaches inclusion of nitric oxide adduct in portion of the device as well as in the coating, the reference does not explicitly teach including two different nitric oxide donors in the same device.

Sogo et al. teach that S-nitroso-N-acetyl-D,L-penicillamine and S-nitrosoglutathione produce more relaxation of vessel walls than commonly used NO donors, and more specifically, teach that the relaxation caused by S-nitroso-N-acetyl-D,L-penicillamine was more sustained, and S-nitrosoglutathione selectively dilates human arteries in vitro and in vivo, and their use might improve the outcome of coronary artery bypass (page 1237, left col.; page 1241, right col.; page 1243, left col.).

Therefore, Sogo et al. recognized administration of two different nitric oxide donors simultaneously, and US '479 recognized inclusion of two nitric oxide donors in single device in different portions, e.g. device itself and its coating.

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide vascular medical device comprising more than one NO donor compounds included in portion of the device and in coating of the same device as taught by US '479, and select S-nitroso-N-acetyl-D,L-penicillamine and S-nitrosoglutathione taught by Sogo et al. to be included in the same device. One would have been motivated to do so because Sogo et al. teach that combination of these two NO donor compounds produce more relaxation of vessel walls than commonly used NO donors with prolonged sustained relaxation and dilatation of human arteries, and their use might improve the outcome of coronary artery bypass. One would have reasonably expected formulating vascular medical device comprising S-nitroso-N-acetyl-D,L-

penicillamine and S-nitrosoglutathione, one is incorporated in a portion of the vascular device and one in the coating of the device to successfully provide prolonged sustained relaxation and dilatation of human arteries, with improvement on the outcome of coronary artery bypass.

The combination of the references teaches the same first nitric oxide donor and second nitric oxide donor as instantly claimed, therefore, the half-life, activity, release rates, and susceptibility to metal ion catalyst release are expected to be the same as those recited by the instant claims.

Regarding claims 40 and 41, it is expected that that the release of the nitric oxide to be faster in circulating blood than to the vascular tissue.

Response to Arguments

4. Applicant's arguments filed 07/15/2009 have been fully considered but they are not persuasive.

Applicants argue that the claimed invention is structurally different from the device of Stamler because nowhere in Stamler is it taught or suggested to employ first and second chemically distinct polymer matrices, each having a nitric oxide donor disposed therein, much less a first polymer matrix having a first nitric oxide donor disposed therein and a second polymer matrix having a second nitric oxide donor disposed therein that differs from the first nitric oxide donor.

In response to this argument, it is argued that Stamler teaches a medical device that is made such that at least a portion of it which come in contact with blood or

vascular tissue includes nitric oxide adduct (col.9, lines 48-52). The nitric oxide adduct can be incorporated into synthetic or natural matrix which is then used to coat those same contact surfaces of the device (col.9, lines 57-60). Therefore, the nitric oxide adduct can be incorporated in portion of the vascular device and or in the coating of the device, i.e. two different matrices. Furthermore Stamler teaches incorporation of second therapeutic agent that has anti-thrombogenic effect along with NO adduct in the coating or linked to the reactive sites in or on the body of the device (col.4, lines 65-67; col.5, line 66 till col.6, line 15). Therefore, at the time of the invention Stamler recognized providing NO adduct in a coating of a device, and also recognized providing NO adduct in the material forming the device, and recognized administering nitric oxide adduct in combination with active agent that can be linked to the surface of the device. The teaching of Stamler would have suggested to one having ordinary skill in the art at the time of the invention to deliver two active agents that could be two NO adducts from one device. The references further suggested presence of NO adduct as coating on the device and another anti-thrombogenic agent linked to the surface of the device and one having ordinary skill in the art would have replaced the second active agent with another NO adduct, specially in view of the teaching of Sogo of the benefits of NO adducts. With all the teachings of Stamler, it is not a difficult task to one versed in the art to arrive to the present invention providing device comprising two different nitric oxide adducts, one is incorporated in the material of the device itself and the other is incorporated in the coating. It has been held that duplication, reversal or rearrangement of parts was held to be an obvious expedient. One having ordinary skill in the art would have incorporate or

combine two NO adducts known to be used for the same purpose in one device in order to achieve additive or synergistic effect obtained by applying one device which is more economic and convenient to the patient and treating medical staff. *In re Gazda*, 219 F.2d 449, 104 USPQ 400 (CCPA 1955); *In re Japikse*, 181 F.2d 1019, 86 USPQ 70 (CCPA 1950); *In re Kuhle*, 526 F.2d 553, 188 USPQ 7 (CCPA 1975).

Applicants argue that Sogo et al. does not remedy this deficiency in Stamler et al. Specifically, Sogo et al. does not teach or suggest first and second chemically distinct polymer matrices, each having a nitric oxide donor disposed therein. Nor does Sogo et al. teach or suggest the use of first and second nitric oxide donors that differ from one another in a single device. Sogo et al. describes four NO donor drugs, however, nowhere in Sogo et al. is it taught or suggested that these drugs may be used in the same device. Sogo et al. may refer to "RIG200 and GSNO" collectively and "GTN and SNP" collectively as "NO donor drugs" but does not teach or suggest that these drugs may be used in the same device. Nowhere in Sogo et al. is a combination of NO donor compounds described. Rather, Sogo et al. presents nitrosoglutathione and N-(S-nitroso-N-acetylpenicillamine) as alternatives, rather than as a combination.

In response to this argument, it is argued that Sogo is relied upon for teaching S-nitroso-N-acetyl-D,L-penicillamine and S-nitrosoglutathione produce more relaxation of vessel walls than commonly used NO donors. More specifically Sogo teaches that the relaxation caused by S-nitroso-N-acetyl-D,L-penicillamine was more sustained, and S-nitrosoglutathione selectively dilates human arteries in vitro and in vivo, and their use

might improve the outcome of coronary artery bypass. Therefore, Sogo recognized and suggested administration of two different nitric oxide donors simultaneously to improve more than one function in coronary patients. Sogo does not teach nitrosoglutathione and N-(S-nitroso-N-acetylpenicillamine) as alternatives, rather teach the two adducts provide two different beneficial effects to the coronary patient. One having ordinary skill in the art would have combined both for the benefits taught by Sogo. Medical devices having two portions made of two different polymers are taught by Stamler. Stamler further teaches combination of active agents with NO adduct in different parts of the medical device. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide vascular medical device comprising NO donor compounds included in portion of the device or in coating of the device and further comprising active agent linked to the active sites in or on the device as taught by US '479, and replace the active agent with S-nitroso-N-acetyl-D,L-penicillamine and S-nitrosoglutathione taught by Sogo et al. to be included in or on the device. One would have been motivated to do so because Sogo et al. teach the benefit of these NO donor compounds to produce more relaxation of vessel walls than commonly used NO donors with prolonged sustained relaxation and dilatation of human arteries, and their use might improve the outcome of coronary artery bypass. One would have reasonably expected formulating vascular medical device comprising S-nitroso-N-acetyl-D,L-penicillamine and S-nitrosoglutathione, one is incorporated in a portion of the vascular device or in its coating and one is linked in or on device to successfully provides

prolonged sustained relaxation and dilatation of human arteries, with improvement on the outcome of coronary artery bypass.

Applicants further argue that the addition of the disclosure of Sogo to that of Stamler on its face relies upon the use of undue hindsight, which is prohibited. The combination is based upon applicant's own disclosure, rather than the teachings within Sogo and Stamler. The courts have been clear that there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. Applicants state that the Examiner has not provided a rational underpinning to support the combination of two different NO donor compounds in two matrices.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Further, the present invention as a whole is taught by the combined teachings of Stamler and Sogo. The incorporation of active agents, including NO adduct, in different portions of a device is taught by Stamler as the reference teaches device made of polymer and coating of different polymer and teaches inclusion of NO adduct in either

the coating or the device itself. Stamler further suggested two active agents in the device, one is NO adduct that can be coated or incorporated into the device, and the second is active agent that has anti-thrombogenic effect that can be linked in or on the device. From the teaching of Stamler, one having ordinary skill in the art would have incorporate or combine two NO adducts known to be used for the same purpose in one device in order to achieve additive or synergistic effect obtained by applying one device which is more economic and convenient to the patient and treating medical staff. Sogo is relied upon for teaching specific NO adducts.

The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, suggestion and motivation to combine the references exist in both references as set forth in this office action.

In considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally

available to one of ordinary skill in the art. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve different problem. It is not necessary that the prior art suggest the combination or modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972).

It has been held that “When a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious.” *KSR Int 'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740 (2007) (quoting *Sakraida v. AG Pro, Inc.,* 425 U.S. 273,282 (1976)). "When the question is whether a patent claiming the combination of elements of prior art is obvious,” the relevant question is “whether the improvement is more than the predictable use of prior art elements according to their established functions.” In addition, "To determine whether there was an apparent reason to combine the known elements in the way a patent claims, it will often be necessary to look to interrelated teachings of multiple patents; to the effects of demands known to the design community or present in the marketplace; and to the background knowledge possessed by a person having ordinary skill in the art. To facilitate review, this analysis should be made explicit. But it need not seek out precise teachings directed to the challenged claim's specific subject matter, for a court can consider the inferences and creative steps a person of ordinary skill in the art would employ". Pp. 11-14. KSR INTERNATIONAL CO. v. TELEFLEXINC. ET AL. (2007).

Finally, a conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969).

In the light of the foregoing discussion, the Examiner's ultimate legal conclusion is that the subject matter as a whole as defined by the claims would have been prima facie obvious within the meaning of 35 U.S.C. 103 (a).

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis A. Ghali whose telephone number is (571) 272-

0595. The examiner can normally be reached on Monday-Thursday, 6:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571) 272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Isis A Ghali/

Primary Examiner, Art Unit 1611

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